

Remarks

Upon entry of the foregoing amendments, claims 6-20 are pending in the application, with claims 6 and 12 being the independent claims. Claims 1-5 were previously sought to be cancelled. Claim 6 has been amended to add the name of the compound of formula (I) as suggested by the Examiner. New claims 12-20 are sought to be added. Support for new claims 12-20 can be found in the originally filed claims and throughout the specification. These amendments do not add new matter and their entry is respectfully requested.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

I. Supplemental Information Disclosure Statement

Applicants note that a Third Supplemental Information Disclosure Statement is submitted accompanying this Amendment and Reply. Applicants respectfully request the Examiner initial and return a copy of Information Disclosure Statement Forms.

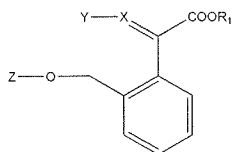
II. Rejection under 35 U.S.C. § 103(a)

Claims 6-11 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Isenring *et al.* (U.S. Patent No. 6,407,100) ("Isenring") and Jautelat *et al.* (U.S. Patent No. 5,789,430) ("Jautelat"). Applicants respectfully traverse this rejection.

A. Prima Facie Case of Obviousness Has Not Been Established

a. Summary of the Cited References

Isenring generally discloses compounds of formula I (encompassing trifloxystrobin), which have fungicidal actions and can be used for controlling or preventing fungal attack:



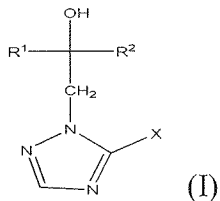
I

(Isenring, col. 1, lines 8-43; and col. 6, lines 34-37.) Isenring also specifically discloses 158 compounds (Examples 1-7, 7a and 8-157), including trifloxystrobin (Example 24). (*Id.* at col. 9, line 64, through col. 19, line 66, Tables 1-3.) Isenring further discloses biological activities of some of these compounds against fungi attack. (*Id.* at col. 21, line 21, through col. 23, line 51.) In addition, Isenring generally states that:

Besides the active compounds of the formula I, the fungicidal compositions according to the invention can also comprise other active compounds, for example other types of fungicidal compositions, insecticidal and acaricidal compositions, bactericides, plant growth regulators and fertilisers. Such combination compositions are suitable for broadening the spectrum of action or for specifically influencing plant growth.

(*Id.* at col. 8, lines 46-53.) However, Isenring does not disclose any particular other active compounds, nor any particular combinations with other active compounds. Thus, at most, Isenring discloses trifloxystrobin, which can be combined with other active compounds.

Jautelat generally discloses triazolyl derivatives of formula (I) (encompassing prothioconazole), which have microbicidal actions and can be used to control undesirable microorganisms:



(I)

(Jautelat, Abstract.) Jautelat also specifically discloses 70 compounds, including prothioconazole (Preparation Example 1) (*id.* at col. 14, line 27, through col. 21, line 42, Table 1; col. 35, lines 10-20; and col. 38, line 32, through cols. 39 and 40, Table 2). Jutelat further generally states that:

When used in plant protection, the active compounds according to the invention can be used as such or, in their formulations, also as a mixture with known fungicides, bactericides, acaricides, nematocides or insecticides, for example so as to widen the spectrum of action or to prevent the build up of resistance. In many cases, this results in synergistic effects, i.e. the activity of the mixture exceeds the activity of the individual components.

(*Id.* at col. 32, lines 24-31.) Jautelat then lists numerous fungicides, bactericides, insecticides, acaricides and nematocides as "suitable components" for the mixture. One of the listed fungicides is tebuconazole. (*Id.* at col. 32, line 32, through col. 34, line 23.) However, Jautelat does not disclose any particular combinations, much less a combination of prothioconazole and tebuconazole. Thus, at most, Jautelat discloses prothioconazole, which can be combined with a laundry list of other active compounds.

b. Claims 6-11 Art Not Prima Facie Obvious over the Cited References

In rendering the rejection, the Examiner stated that Isenring teaches trifloxystrobin as a fungicide; Jautelat teaches prothioconazole and tebuconazole as microbicides; and instant specification discloses that all three compounds used in the combination are known. The Examiner then concluded:

Since all the above cited reference teach the active compounds as claimed it is *prima facie* obvious to combine two or more compositions each of which is taught by the prior art to be useful for the same purpose in order to form a new composition that is to be used for the very same purpose; the idea of combining them flows logically from their having been individually taught in the prior art. In re Kerkhoven, 205 USPQ 1069.

(Office Action, page 6). Applicants respectfully disagree.

Applicants reiterate that for the reasons detailed in Applicants' Replies of May 1, 2006, October 26, 2006, January 29, 2007, August 22, 2007, January 17, 2008, April 3, 2008, and December 9, 2008, claims 6-11 are not *prima facie* obvious in view of the cited references.

Claims 6-11 are directed to an active compound combination comprising trifloxystrobin, prothioconazole and tebuconazole, which possesses a synergistic effect. Each of claims 6-11 also requires particular mixing ratios of trifloxystrobin to prothioconazole, and trifloxystrobin to tebuconazole to achieve the synergistic effect. Claim 11 further recites specific fungi to be controlled by the claimed combinations.

As discussed above, taken together, Isenring and Jautelat, at most, teach that trifloxystrobin can be combined with other active compounds; and prothioconazole can be combined with other active compounds. However, there is nothing in the cited references that would provide a reason for making the three-compound combination, comprising trifloxystrobin, prothioconazole and tebuconazole, as recited in the present claims 6-11. Also, the instant specification merely states that all three active compounds (*i.e.*, trifloxystrobin, prothioconazole and tebuconazole) were individually known in the art. The instant specification does not admit that the three-compound combination, comprising trifloxystrobin, prothioconazole and tebuconazole, would have been obvious as suggested by the Examiner. To the contrary, the instant specification states that "[s]urprisingly, the fungicidal action of the active compound combination according to the invention comprising the three active compounds is considerably higher than the sum of the actions of the individual active compounds. . . ." (*see* the Specification, page 2 lines 19 -21).

Furthermore, claims 6-11 require particular mixing ratios of trifloxystrobin to prothioconazole and trifloxystrobin to tebuconazole. Neither Isenring, nor Jautelat discloses or provides a reason to select the mixing ratios as recited in claims 6-11. Thus, the mixing ratios as recited in claims 6-11 were not known in the cited references. In rendering the rejection, the Examiner did not even address the mixing ratios. Applicants respectfully submit that to establish a *prima facie* case of obviousness of a claimed invention, all claim limitations must be considered (*see* M.P.E.P. § 2143.03).

Applicants are aware of the flexible approach for establishing obviousness set out in *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398 (2007). However, as cautioned by Judge Rader in a post-*KSR* decision in *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009), "where a

defendant merely throws metaphorical darts at a board filled with combinatorial prior art possibilities, courts should not succumb to hindsight claims of obviousness." (561 F.3d at 1359.) In rendering the rejection, the Examiner selected trifloxystrobin disclosed in Isenring, and found prothioconazole and tebuconazole by picking and choosing from a vast number of optional mixing partners disclosed in Jautelat, based on impermissible hindsight. Furthermore, even if one would have picked and chosen presently claimed combination, one would not have any expectation other than merely additive effect of the combination. As such, Applicants contend that the Examiner's rejection is based on impermissible hindsight.

The Examiner cited *In re Kerkhoven* to support the rejection. Applicants respectfully submit that the facts in the present application are far removed from *In re Kerkhoven*, and thus its holding should not be broadly applied to the present invention for the following reasons.

In re Kerkhoven dealt with the patentability of claims directed to a process of preparing a spray-dried detergent by mixing together spray-dried nonionic detergents and anionic detergents. *In re Kerkhoven*, 205 U.S.P.Q. 1069 (CCPA 1980). According to the United States Court of Customs and Patent Appeals ("CCPA"), the appealed claims "require no more than the mixing together of two conventional spray-dried detergents." *Id.* at 1072. Applicants note that the appealed claims in *In re Kerkhoven* only require combining a spray-dried nonionic detergent with a spray-dried anionic detergent, and do not require combining a specific nonionic detergent with a specific anionic detergent. Hence, the holding of *In re Kerkhoven* cannot be broadly applied to the present invention because, contrary to the facts in *In re Kerkhoven*, the present claims 6-11 require combining three specific fungicides, trifloxystrobin, prothioconazole and tebuconazole, within specific ranges of mixing ratios that provide synergistic effect. In sum, because the facts in *In re Kerkhoven* are not analogous to that of the present invention, its holding should not be broadly applied to the present invention.

Accordingly, for at least these reasons, the Examiner has not established a *prima facie* case of obviousness of claims 6-11. Applicants respectfully request the Examiner reconsider and withdraw the rejection.

c. Claims 12-20 Art Not Prima Facie Obvious over the Cited References

New claims 12-20 are directed to a synergistically effective composition consisting essentially of trifloxystrobin, prothioconazole and tebuconazole, and optionally one or more extenders, surfactants or a combination thereof; and a method of controlling fungi by the composition. Each of claims 12-20 also requires particular mixing ratios of trifloxystrobin to prothioconazole, and trifloxystrobin to tebuconazole to achieve the synergistic effect. Claims 18-20 further recite specific fungi to be controlled by the claimed composition.

For the same reasons stated above, claims 12-20 are not *prima facie* obvious over Isenring in view of Jautelat.

B. Synergistic Effect

Even assuming, *arguendo*, that a *prima facie* case of obviousness had been established, which it has not, the synergistic effect exhibited by the claimed invention is sufficient to rebut a *prima facie* case of obviousness.

Applicants reiterate that for the explanations detailed in Applicants' Replies of May 1, 2006, October 26, 2006, January 29, 2007, August 22, 2007, January 17, 2008, April 3, 2008, and December 9, 2008, the present invention possesses synergistic effect as shown in the specification and the Declaration of Dr. Peter Dahmen ("the Declaration"), and as demonstrated by different methods of determining synergistic effect.

However, the Examiner did not consider the data presented in the specification and the Declaration synergism. Specifically, the Examiner asserted that:

The difference in synergistic efficacy 78 and compound of formula 1 (trifloxystrobin) efficacy 67 does not represent

synergism. The data presented in Table A on page 11 of the specification is *Pyrenophora teres* test on barley (declaration includes two more examples). The synergism as claimed cannot be predicted for the effect on any other phytopathogenic fungi. The [sic] Furthermore, the data does not commensurate with the scope of claims.

* * *

In example 1 [the Declaration] the calculated efficacy 67 and found 78 is not synergistic for *Blumeria graminis*. Example 2 appears to be marginal synergistic for *Fusarium culmorum*. It is clear from the data that the ratio of the three compounds as 1:1:1 does not necessarily will act as synergistic on all the fungi. . . The combination of the known compounds is considered obvious to one skilled in the art as the difference in efficacy of individual compound of formula I (67) and the mixture of three components (78) is not synergistic.

* * *

The data presented in the specification and in the declaration does not commensurate to the scope of claimed subject mater and does not show any synergism.

(Office Action, pages 6-8.) Applicants respectfully disagree.

First, with respect to the data in the specification and the Declaration, the Examiner compared the efficacy of the claimed combination with trifloxystrobin used alone. The Examiner's method is not an appropriate method for finding synergism or lack thereof in view of *In Re Luvisi*, where the court defines the synergism to mean "the combined action of two or more agents * * * that is greater than the sum of the action of one of the agents used alone * * * ." *In Re Luvisi*, 144 U.S.P.Q. 646, 652 (CCPA 1965). Thus, the proper method for finding synergism or lack thereof is by comparing the efficacy of the claimed combination with the sum of efficacy of trifloxystrobin, prothioconazole and tebuconazole used alone, as illustrated and explained in details in Applicants' Replies of January 29, 2007, August 22, 2007, January 17, 2008, April 3, 2008, and December 9, 2008.

Second, in *In re Kollman*, the CCPA stated that "the unobviousness of a broader claimed range can, in certain instances, be proven by a narrower range of data. Often, one having ordinary skill in the art may be able to ascertain a trend in the exemplified

data which would allow him to reasonably extend the probative value thereof." *In re Kollman*, 595 F.2d 48, 56 (CCPA 1979). In the present application, Applicants have demonstrated synergistic effect of the claimed invention at different mixing ratios, against different fungi and on different crops/plants. A person of ordinary skill in the art would have been able to ascertain a trend in the exemplified data to reasonably extend such data to a broader claimed range as recited in claim 6. In addition, claims 7 and 10 are directed to a synergistically effective active compound combination, comprising trifloxystrobin to prothioconazole and tebuconazole, wherein the mixing ratio of trifloxystrobin to prothioconazole is from 1:0.2 to 1:5 (claim 7), or is 1:0.85 (claim 10); and the mixing ratio of trifloxystrobin to tebuconazole is from 1:0.2 to 1:5 (claim 7), or is 1:1 (claim 10), respectively. Claims 7 and 10 are much narrower in scope as compared to claim 6. In view of the evidences of unexpected synergistic effect presented in the specification and the Declaration, a person of ordinary skill in the art would have been able to ascertain a trend in the exemplified data to reasonably extend such data to the claimed range as recited in claims 7 and 10. Similarly, claim 11 is directed to method for controlling *Pyrenophora* or *Fusarium* by using the combination according to claim 6. Applicants have demonstrated the unexpected synergistic effect obtained with claimed combination against *Pyrenophora* or *Fusarium*. Accordingly, Applicants respectfully submit that the evidence of unexpected synergistic effect presented in the specification and the Declaration at least commensurates with the scope of claims 7, 10 and 11.

Finally, the Examiner questioned the validity of the Colby formula, citing *Ex parte Quadranti* (see Office Action, pages 8 and 9). Applicants do not rely solely on the Colby formula to demonstrate synergism, rather Applicants have demonstrated the synergistic effect of the claimed invention by using various methods as set forth in Applicants' Replies of May 1, 2006, October 26, 2006, January 29, 2007, August 22, 2007, January 17, 2008, April 3, 2008, and December 9, 2008.

Furthermore, in a Second Information Disclosure Statement dated August 10, 2009, Applicants submitted a total of 24 articles describing the use of the Colby formula in calculating expected efficacies of herbicide combinations. For example, in Bauer *et*

al., "Response of Selected Weed Species to Postemergence Imazethapyr and Bentazon," *Weed Tech.* 9:236-242 (1995), "[f]or the herbicide combinations, the expected weed control value was calculated following Colby's method (4)" (*id.* at page 237); in Blackshaw *et al.*, "Herbicide Combinations for Postemergent Weed Control in Safflower (*Carthamus tinctorius*)," *Weed Tech.* 4: 97-104 (1990), "[p]lant responses to herbicide combinations were determined using Colby's method (9)" (*id.* at page 98); in Bradley *et al.*, "Response of Sorghum (*Sorghum bicolor*) to Atrazine, Ammonium Sulfate, and Glyphosate," *Weed Tech.* 14: 15-18 (2000), "[e]xpected values for herbicide interactions were calculated using the Colby equation (Colby 1967)" (*id.* at page 16); Burke, *et al.*, "CGA-362622 Antagonizes Annual Grass Control with Clethodim," *Weed Tech.* 16: 749-754 (2002), "[t]he expected response for herbicide mixtures and sequential treatments was calculated according to Colby (1967)" (*id.* at page 751); in Gillespie, G.R. & Nalewaja, J.D., "Wheat (*Triticum aestivum*) Response to Triallate Plus Chlorsulfuron," *Weed Tech.* 3:20-23 (1989), "[e]quations previously described by Colby (3) were used to indicate synergistic or antagonistic interactions following the application of various triallate plus chlorsulfuron treatments" (*id.* at page 20); in Green *et al.*, "Metribuzin and Chlorimuron Mixtures for Preemergence Broadleaf Weed Control in Soybeans, *Glycine max*," *Weed Tech.* 2: 355-363 (1988), "[m]ixture observations were compared to the expected responses predicted by Colby's equation (6, 9)" (*id.* at page 356); in Harker, N.K., & O'Sullivan, P.A., "Synergistic Mixtures of Sethoxydim and Fluazifop on Annual Grass Weeds," *Weed Tech.* 5: 310-316 (1991), "Colby's method was used to predict 'Expected' plant responses to herbicide combinations" (*id.* at page 311); in Lanclos *et al.*, "Glufosinate Tank-Mix Combinations in Glufosinate-Resistant Rice (*Oryza sativa*)," *Weed Tech.* 16: 659-663 (2002), "[i]nteractions between herbicide mixtures were calculated by the mathematical method described by Colby (1967)" (*id.* at page 660); in Norris *et al.*, "Weed Control from Herbicide Combinations with Three Formulations of Glyphosate," *Weed Tech.* 15: 552-558 (2001), "[t]he method described by Colby (1967) was used to calculate the expected values of control from herbicide combinations" (*id.* at page 554); in Palmer *et al.*, "Broadleaf Weed Control in Soybean (*Glycine max*) with CGA-277476 and Four Postemergence Herbicides," *Weed Tech.* 14: 617-623 (2000), "[t]he method described by Colby (1967) was used to calculate expected levels of control

from herbicide tank mixtures" (*id.* at page 619); in Scott *et al.*, "Spray Adjuvant, Formulation, and Environmental Effects of Synergism from Post-Applied Tank Mixtures of SAN 582H with Fluazifop-P, Imazethapyr, and Sethoxydim," *Weed Tech.* 12: 463-469 (1998), "[t]he method described by Colby (1967) was used to calculate interactions of herbicide tank mixtures" (*id.* at page 465); in Shaw, D.R. & Arnold, J.C., "Weed Control from Herbicide Combinations with Glyphosate," *Weed Tech.* 16: 1-6 (2002), "Colby's (1967) method was used to calculate synergistic, antagonistic, or additive responses of herbicide tank mixtures" (*id.* at page 2); in Zhang *et al.*, "Fenoxaprop Interactions for Barnyardgrass (*Echinochloa crus-galli*) Control in Rice," *Weed Tech.* 19: 293-297 (2005), "[i]nteractions between fenoxaprop and other herbicides were calculated by the mathematical method described by Colby (1967)" (*id.* at page 294); and in Flint *et al.*, "Analyzing Herbicide Interactions, A Statistical Treatment of Colby's Method," *Weed Tech.* 2: 304-309 (1988), the authors stated that "[t]he use of Colby's method is desirable because most researchers understand the concept and assumptions" (*id.* at page 307).

As summarized above, the Colby formula is a widely accepted method for calculating synergistic, antagonistic or additive effect of herbicide mixtures by a person of ordinary skill in the art. The Examiner has provided no evidence to the contrary.

For the reasons set forth above, Applicants respectfully request that the Examiner reconsider the evidence of unexpected synergistic effect presented in the specification and the Declaration, and that the rejection be withdrawn.

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

Sterne, Kessler, Goldstein & Fox p.l.l.c.



Lei Zhou

Attorney for Applicants

Registration No. 48,291

Date: February 22, 2010

1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600

1078672_1.DOC